RESEARCH ON RAYNAUD'S PHENOMENON AND SYSTEMIC SCLEROSIS

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National Institute of Arthritis and Musculoskeletal and Skin Diseases

PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invites research grant applications for studies of basic biological and clinical aspects of Raynaud's phenomenon, focusing particularly on microvascular control mechanisms, collagen synthesis, and other aspects of fibroblast biology, endothelial cell function, and immunological abnormalities associated with Raynaud's phenomenon. The goal of this program announcement (PA) is to promote research that contributes to the understanding the pathogenesis of Raynaud's phenomenon and its relationship to other pathogenetic mechanisms in systemic sclerosis.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Research on Raynaud's Phenomenon and Systemic Sclerosis, is related to the priority area of chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001- 00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private institutions, such as universities, colleges, hospitals, laboratories, units of State

and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) awards (R29).

MECHANISM OF SUPPORT

Applications are requested under the following mechanisms: traditional research grants (R01), FIRST awards (R29). Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will vary also.

RESEARCH OBJECTIVES

The goal of this PA is to encourage research that will elucidate the relationship between Raynaud's phenomenon and systemic rheumatic illness. Raynaud's phenomenon consists of intermittent blanching, reactive hyperemia, and cyanosis of fingers, toes, ears, and nose in response to cold, emotion, and other external events. More than 90 percent of patients with scleroderma (systemic sclerosis) and approximately 25 percent of patients with systemic lupus erythematosus develop Raynaud's phenomenon, often as the first symptom, but the relationship between this abnormality and the associated rheumatic illness remains unknown. Recent studies have suggested that the primary abnormality may reside in control mechanisms for microvascular blood flow, endothelial cell injury, or pathologic biology of endothelial cells or fibroblasts. In scleroderma, Raynaud's phenomenon is closely associated with excessive skin fibroblast synthesis of skin collagen. Several autoantibodies occur in patients with scleroderma and with systemic lupus erythematosus; whether these autoantibodies cause, follow, or are unrelated to the occurrence of Raynaud's phenomenon is unknown.

Research proposed in response to this Program Announcement may be at any level of biological organization, but must in some way address the pathophysiology of Raynaud's phenomenon and/or its relationship to systemic sclerosis or other rheumatic disease. Possible topics include, but are not limited to, the following:

o Up- and down-regulator mechanisms of microvascular blood flow;

o Neurogenic mechanisms in microcirculatory abnormalities;

o Immunologically-mediated endothelial cell injury;

o Control mechanisms of fibroblast function as it relates to the occurrence of scleroderma; and

o Relationship of specific autoantibodies to Raynaud's phenomenon.

STUDY POPULATIONS
SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded.

However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided. Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines as indicated in the application kit. Application kits are available at most institutional offices of sponsored research and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the PA must be typed in Section 2a on the face page of the application.

The completed original application and five legible copies must be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

REVIEW PROCEDURES

Applications will be assigned on the basis of established PHS referral guidelines. Applications will be reviewed for scientific and technical merit by initial review groups (study sections) of the Division of Research Grants (DRG), NIH, in accordance with the standard NIH peer review procedures.

Following scientific-technical review, the applications will receive a second-level review by the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council or by other relevant advisory boards and/or councils.

AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to NIAMS. The following will be considered in making funding decisions:

- quality of the proposed project as determined by peer review;
- availability of funds; and
- program balance among research areas of the announcement.

INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:
Director, Arthritis Program
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 405
Bethesda, MD 20892
Telephone: (301) 402-3340

Direct inquiries regarding fiscal matters to:
Diane M. Watson
Chief, Grants Management Branch

National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 732A
Bethesda, MD 20892
Telephone: (301) 402-3352

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 410, 78th Congress, as amended, 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

Return to 1992 Index
Return to NIH Guide Main Index